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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MARK E. FEJER
GAS TECHNOLOGY INSTITUTE
1700 SOUTH MOUNTAIN PROSPECT ROAD
DES PLAINES, IL 60018

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,105	KAYSER ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *15-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/02, 3/02, 06/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, claims 1-14, in the reply filed on 01/03/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-14 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2, lines 3-4, the phrase "TT medium agar plates" renders the claim vague and indefinite because the meaning of the phrase is unclear. The specification does not provide a definition for this phrase. Claims 3 and 4 which depend from claim 2 are also rejected because they do not correct the defect of claim 2.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 7-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with

the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of claims 7-14 are genus claims directed toward: a genus of any "maintenance means for maintaining plasmids", a genus of any *"Thermus* promoter sequences, a genus of any 5' untranslated region (UTR) added to a 5' end of a transcript which increases gene expression and mRNA stability/longevity", a genus of any ribosomal binding site (RBS), a genus of any inducible promoter, a genus of any multiple cloning sites, and a genus of any "*Thermus* transcriptional termination sequence". The scope of each genus include many nucleic acid sequences with widely differing structural, chemical, and physical characteristics. Furthermore, each genus is highly variable because a significant number of structural differences between genus members exists.

The specification discloses the *Thermus* inducible promoter of SEQ ID NO: 5, a 5' UTR of SEQ ID NO: 2, a RBS of SEQ ID NO: 3 and 4, and a Thermus transcriptional terminator of SEQ ID NO: 1. However, the specification fails to provide a written description of additional genus members of each of the claimed genera of claims 7-14. Neither the specification nor the general knowledge of those skilled in the art provide evidence of any nucleotide sequence and structure which would be expected to be common to the members of each claimed genus. A sufficient written description of the claimed genus of inducible promoters, for example, may be achieved by a recitation of a representative number of defined by nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the necessary common features or attributes possessed by members of each genus claimed in claims 7-14. Accordingly, Applicants has failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicant was in possession of the claimed invention of claims 7-14.

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in

> section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 5-8, 10, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshima et al. (Int. J. Syst. Bacteriol. 1974 Jan; 24(1): 102-112) in view of Hoshino et al. (Appl Environ Microbiol. 1993 Sep;59(9):3150-3).

Oshima et al. teach a process comprising collecting samples of thermophilic microorganisms from hot springs in Japan, identifying and separating strain *Thermus thermophilus* HB8 which produces yellow pigments, and growth of these stains on agar plates at 60°C (see entire reference, especially **Culture media** section on p. 103, and **RESUTS** section pp. 104-109).

Claims 1, 5-8, 10, and 12 differ from the teachings of Oshima et al. in that Oshima et al. does not teach a process step of mutating by recombinant means, introducing a gene of interest suitable for producing a protein of interest, a *Thermus* promoter sequence, a ribosomal binding site (RBS), and at least one multiple cloning site.

Hoshino et al. teach a process comprising mutating *Thermus thermophilus* HB27 host cells by transformation with a *Thermus* plamid pYK134 containing a *Thermus* promoter sequence adjacent to the *crtB* gene, a multiple cloning site containing a *Hin*dIII site, and inherently has a RBS (which promotes efficient and accurate translation of mRNA) as evident by overproduction of the *crtB* gene products and the production of three times the amount of carotenoid as that produced by an untransformed host cell (see entire publication, especially Fig. 1, and pp. 3150-3152).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the process of Oshima et al. such that the *Thermus thermophilus* HB8 is mutated by transformation with *Thermus* plamid pYK134 taught by Hoshino et al. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of having a beneficial method that produces carotene-related pigments.

No patentable weight is given to the preamble of process claims 1, 6-8, 10, and 12 since it merely recites the purpose of these process claims. Thus, the process steps of the modified Oshima et al. process stated above renders the claims obvious because these process steps are the same as the process steps of claims 1, 6-8, 10, and 12. Because the process steps of the modified

Oshima et al. process stated above are the same as the process steps of claims 1, 6-8, 10, and 12, then the modified Oshima et al. process would inherently produce the thermophilic microorganism GTI-CARD recited in claim 5 and carotene-related pigments recited in claims 1, 6-8, 10, and 12.

9. Claims 9, 11, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshima et al. in view of Hoshino et al. as applied to claims 1, 5-8, 10, and 12 above, and further in view of Castan et al. (J Bacteriol. 2001 Feb;183(4):1491-4) and Osipiuk et al. (Biochim Biophys Acta. 1997 Sep 12;1353(3):253-65).

The teachings of Oshima et al. and Hoshino et al. have been stated above.

Castan et al. teach the 5' untranslated region (5' UTR) of the S-layer gene *slpA* from *Thermus thermophilus* HB8 and that the said 5' UTR of the S-layer gene *slpA* from *Thermus thermophilus* HB8 stablilzes the mRNA based on the leader mRNA forming a highly folded structure (see entire publication, especially Fig. 1, and p1493, left column, **Conclusions** section)

Osipiuk et al. teach a heat-shock inducible promoter of the *dnaK* operon of *Thermus thermophilus* HB8 which is composed of three functionally linked genes of *dnaK, grpE*, and *dnaJ*; and strong transcription termination sequences between the *dnaK* and *grpE* genes (see entire publication, especially Fig. 1, and p. 256-264).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the modified process of Oshima et al. in view of Hoshino et al. stated above by inserting the 5' UTR of the S-layer gene *slpA* from *Thermus thermophilus* HB8 taught by Castan et al., the heat-shock inducible promoter of the *dnaK* operon of *Thermus thermophilus* HB8 taught by Osipiuk et al., and the strong transcription termination sequence between the the *dnaK* and *grpE* genes taught by Osipiuk et al. into the *Thermus* plasmid pYK134 taught by Hoshino et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to insert the 5' UTR of the S-layer gene *slpA* from *Thermus thermophilus* HB8 taught by Castan et al. in order to stablize the *crtB* mRNA transcribed from the *Thermus* plasmid pYK134. One of ordinary skill in the art at the time the invention was made would have been motivated to insert the heat-shock inducible promoter of the *dnaK* operon of *Thermus thermophilus* HB8 taught by Osipiuk et al. in order to facilitate expression of the *crtB* gene product at an elevated temperature of 85°C. One of ordinary skill in the art at the time the

invention was made would have been motivated to insert the strong transcription termination sequence taught by Osipiuk et al. to prevent trancriptional read-through of the *Thermus* plasmid pYK134 DNA.

10. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshima et al. (Int. J. Syst. Bacteriol. 1974 Jan; 24(1): 102-112) in view of Adelberg et al. (Biochem Biophys Res Commun. 1965; 18(5-6): 788-95).

The teachings of Oshima et al. have been stated above.

Claims 1-4 differ from the teachings of Oshima et al. in that Oshima et al. does not teach a process step of mutating by spreading cells onto agar plates comprising nitrosguanidine (NTG).

Adelberg et al. teach a process for mutagenesis by using the mutagen N-methyl-N'-nitro-N-nitrosoguanidine (NTG) (see entire publication).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the process of Oshima et al. such that the *Thermus thermophilus* HB8 is mutated by growing the strains on agar plates comprising NTG and then separating mutant colonies that over produce carotene. One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of having a beneficial method that produces carotene-related pigments.

No patentable weight is given to the preamble of process claims 1-4 since it merely recites the purpose of these process claims. Thus, the process steps of the modified Oshima et al. process stated above renders the claims obvious because these process steps are the same as the process steps of claims 1-4. Because the process steps of the modified Oshima et al. process stated above are the same as the process steps of claims 1-4, then the modified Oshima et al. process would inherently produce carotene-related pigments recited in claims 1-4.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600